

Effects of the Workplace on Fertility and Related Reproductive Outcomes

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This report reviews the recent literature on the adverse effects of occupational factors on fertility and related reproductive outcomes. Few studies fulfill the criteria of good study design because of small sample size, insensitive measures of effect, selection, recall, and observation bias, weak if any control of confounding factors, bad definition of exposure, inability to analyze a dose-response relationship, and inadequate statistical analysis. The high prevalence of unsuccessful reproductive outcomes in the general population makes the design of human fertility studies difficult. Although a number of publications indicate that certain occupational factors and settings adversely affect both male and female fertility, it is virtually impossible to estimate the proportion of infertility due to occupational factors in the general population. The collected data suggest that the exposure to the following substances or occupational settings may affect a function of male genital system, leading to sperm abnormalities, hyperestrogenism, impotence, infertility, and/or increased spontaneous abortion rate in wives of exposed workers: alkylmercury, antimonide, anesthetic gases, boron, carbon disulfide, chlorodecane, chloroprene, some carbamates (carbaryl), diaminostilbene, 1,2-dibromo-3-chloropropane, ethylene glycol ethers, ethylene dibromide, inorganic lead, manganese, methyl chloride, organic solvents, synthetic estrogens and progestins, tetraethyllead, combined exposure to styrene and acetone, welding operations, and heat. The majority of reviewed papers on female fertility concerns the alterations of menstrual cycle and pregnancy complications rather than occupational exposure-induced female infertility. The literature supports the hypothesis that, in general, working women have a tendency of higher risk of unsuccessful reproductive outcomes, although the existing data are not sufficient.

Introduction

Several years ago, the World Health Organization (WHO) Regional Office for Europe initiated a review and assessment of the existing data on the impact of the working environment on fertility. The literature surveys were prepared by H. Taskinen of the Institute of Occupational Medicine in Helsinki, Finland, and B. Baranski of the Institute of Occupational Medicine in Lodz, Poland. These were assessed by the WHO Working Group at a consultation meeting held in Varna on April 10-12, 1989. The assessment of the data and the conclusions presented in this paper are largely based on the findings reached by this WHO Working Group, although some new data are also taken into consideration.

Reproductive disorders are important health problems. It is estimated that 10-15% of all married couples or couples living together have experienced an infertility problem. Women, men, or couples who remain childless in spite of trying to achieve a pregnancy after 1 year of unprotected sexual intercourse are usually defined in a

clinical setting as being "infertile." Couple fertility may be regarded as the probability of a couple achieving pregnancy each menstrual cycle when no means of contraception are used, and this is called fecundability by demographers (1). Fecundability integrates the effects of several biological processes in the male and female partners and also in the developing conceptus. The fertility of most couples is a voluntary, self-controlled phenomenon.

By studying couple fertility, it is possible to monitor many biological processes indirectly at the same time. The disadvantage of this approach is that these studies may be less sensitive than studies focusing on each part of the process separately. There are other measures that can be studied within the continuum of this disorder either together with, or separately from, the parameters of infertility such as hormonal imbalances, menstrual disorders, changes in the quality of semen, spontaneous abortions prior to the clinical recognition of pregnancy, stillbirth, perinatal death, live birth rate, low birth weight, structural and functional congenital malformations, and childhood cancers. These topics have been subjects of previous WHO reports (2,3). The most sensitive method of examining the effects of exposure to environmental agents on reproduction would be to study several different outcomes at several different exposure levels. The most common outcomes to study would be fetal loss and impaired fertility (4). Epidemiological issues that require special

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consideration within the area of occupational infertility studies include measurement of outcome, potential confounding factors, and assessment of exposure.

Measurement of Infertility

When selecting which specific outcomes of the reproductive process should be measured, it is important to take into consideration relevance, sensitivity, and feasibility to make sure that the actual measurement is a true reflection of fertility, is the most informative in a statistical sense, and is applicable to larger groups of people.

Infertility Rate

These are several definitions of infertility: *a*) failure to produce a live birth after 1 year of unprotected intercourse, which is the demographic definition of infertility. This definition has limited applicability because it fails to take into consideration any of the other possible outcomes such as spontaneous abortion or stillbirth, *b*) inability to conceive after 1 year of unprotected intercourse. This could be considered the ideal definition, but conception is sometimes technically difficult to diagnose even when using the most sensitive methods such as β -human chorionic gonadotropin (hCG) measurements. It is also not very feasible to assess the conception rate in a population setting because it is expensive and requires daily testing, *c*) inability to produce a clinically recognizable pregnancy after 1 year of unprotected intercourse. This is a more practical working definition of infertility for assessing a given population in comparison with a definition that is dependent on the knowledge of conception, and this is the recommended definition of infertility for use in infertility rate studies.

The assessment of infertility rate as a measurement of alteration in the reproductive process has certain methodological advantages and disadvantages that must be taken into consideration when designing, analyzing, and interpreting various studies. Among the advantages are *a*) information is readily available, although problems with recall may be complicating factors; *b*) the end point measured is relevant to the study; and *c*) it is feasible to apply this measurement to large-scale studies because results can be obtained from questionnaires or review of medical case records, and it does not require laboratory investigations. On the other hand, assessing infertility rate has the disadvantage that it does not differentiate between early spontaneous abortion and the inability to conceive. However, similar factors may influence both of these events, and in practical terms they do not need to be differentiated in order to obtain relevant information on reproductive hazards. Factors complicating infertility rate as an end point are that the method of measurement is relatively insensitive, and the intermittent use of contraception has to be taken into account in questionnaire design and analysis.

Time to Pregnancy

The time to pregnancy is defined as the time interval between the start of unprotected intercourse and a

clinically recognizable pregnancy. The cessation of preventive measures usually results in 25% of couples successfully achieving a pregnancy during the first menstrual cycle (5). Counting the number of cycles required to achieve a pregnancy may be a more sensitive measurement than assessing the infertility rate, or assessing the occurrence or spacing of births during the reproductive lifetime (6). Agents such as those causing early abortions disturb the biological processes that are essential for achieving a detectable pregnancy and therefore increase the time required to produce a recognized pregnancy. Although such a delay may only be a few cycles, this method may be sufficiently sensitive to detect statistically significant changes.

An advantage in detecting small increases in average time to pregnancy is that the harmful agent may be recognized before irreversible damage occurs (1). This measurement reflects fecundability and is a more sensitive parameter than the infertility rate, requiring smaller numbers than in infertility studies. Measuring the time to pregnancy appears to be reliable if the pregnancy under consideration is recent, but if the assessment of length of time is dependent on recall estimates, accuracy may be reduced because memory is affected by passage of time. Time to pregnancy studies are also feasible and applicable to the occupational setting where alterations in time to pregnancy pre- and postexposure can be investigated. The disadvantages of time to pregnancy as an end point include: *a*) it totally excludes infertile couples and *b*) recall may not be accurate in retrospective studies if the pregnancy occurred a long time previously.

Number of Pregnancies over a Couple's Reproductive Lifetime

Demographers often count the number of pregnancies achieved by a couple, but this has limited sensitivity in the occupational setting mainly as a result of changing social circumstances such as changing partners and change in family size expectation. These factors almost certainly have a greater impact on number of pregnancies than occupational factors.

Ratio of Expected to Observed Live Births

The standardized birth ratios (SBR) adjusted for parental age, race, calendar time, and parity give an indication of the expected number of live births for a given population. The actual number of live births among female employees and wives of male employees in the time intervals both before and after exposure to occupational agents may be compared with expected numbers based on national statistics. This measurement is relevant and is feasible for large-scale studies, but it is relatively insensitive, and the design and analysis of the questionnaire must take into account the use of contraception. The ratio of expected to observed live births only takes into consideration successful pregnancies producing live births and excludes pregnancies with other outcomes such as spontaneous abortion, which are included among the cases of

reduced fertility. Therefore, this method of assessment may not detect differences in fetal death rates between the exposed and unexposed workers. When employed women are under investigation the controls must also be employed women because in some countries, notably the United States, employment and childbearing in women are closely interrelated (1).

Potential Confounding Factors

There are many extraneous factors that have the potential to confound studies of infertility or pregnancy outcomes and these factors are relevant to the design and/or analysis of the investigations. Such potential confounding factors are *a)* sexually transmitted infections, the determinants of which are thought to be the number of sexual partners and the usage and type of contraception, *b)* sexual activity, taking into consideration both timing and frequency of intercourse. These two factors are probably the major confounders, but other factors must also be considered such as exposure of the spouse to different agents; lifestyle factors which are thought to affect fertility such as smoking, alcohol, caffeine and exercise; general medical conditions; medication including oral progestational steroids; previous recent pregnancy and lactation; socioeconomic status; age; parity; and education. Some of the problems associated with these potential confounders may be addressed, at least in part, by careful study design. The studies must include relevant case controls who are appropriately matched for some of these confounders, necessitating careful control group selection. The reliability of information relating to potential confounding factors, such as sexually transmitted diseases and their determinants, is difficult to confirm. Careful and appropriate control group selection will, however, ameliorate this problem.

Assessment of Exposure

There are many methodological problems in assessing exposure to various agents, including the definition and evaluation of occupational exposure as it applies to the individuals making up the population under survey. Selevan and Lemasters (4) pointed out that the definition and measurement of exposure and dose can limit the ability of the investigation not only to detect a dose-response relationship but also to detect an effect of exposure to a particular agent on fertility and/or sexuality. In population studies it is often only possible to collect information on a single occupational group. This can be useful in identifying subgroups at risk, which can then be the subjects of more detailed toxicological studies. In many situations, workers are exposed to combinations of agents the potential effects of which cannot be separated. Only a summary effect can be detected in these situations, and it is not possible to identify the actions of individual agents.

The nominal scale of exposure subdivides individuals dichotomously into exposed or not exposed groups. The use of this qualitative scale assumes that any exposure or any exposure greater than a defined level may have an

effect. However, the individuals classified into the exposed category may differ significantly in respect of exposure level. The continuous scale of exposure requires precise data on exposure level, taking into account whether exposure is to a single factor or several factors such as a mixture of chemicals, noise, microwaves, etc. Exposure status is sometimes based on only a few measurements, which can result in random misclassification of the presence or absence of exposure and this will introduce bias towards no effect in the results of the study (7).

The ordinal scale of occupational exposure classifies the levels of exposure into categories such as low, medium, or high. Such data can be analyzed either according to dose level, assuming a dose-response relationship, or without assuming a dose-response relationship by comparing each exposure level with an unexposed comparison group.

Occupational Exposure Associated with Infertility

There are many papers in the literature pertaining to occupation or exposure to occupational agents, and the associated effects on fertility and other related reproductive outcomes. Tables 1 and 2 list some of the hazards encountered in the workplace and their possible effects on the reproductive process. The lists are not exhaustive, and a critical evaluation of all the published data on individual agents is not within the scope of this review article.

Some of the substances have been inadequately studied but have been included because of suggestive data. Tables 1 and 2 probably underestimate the number of definite associations because an association is not presented as positive unless the evidence is absolutely unequivocal. For example, a compilation of many different studies gives strong evidence that dibromochloropropane has a pronounced effect on semen quality and fertility, but some conflicting results are sufficient to cast doubt in the present survey.

Occupational Exposure and Female Infertility

The literature data referring to the effects of chemical and physical agents that are present in the working environment and that affect female fertility and related reproductive outcomes are summarized in Table 1. The majority of the papers cited in this table describe alterations in the menstrual cycle or early and late pregnancy complications rather than giving details of female infertility induced by exposure to occupational agents. Many of the publications report on cycle length and duration of menstrual flow, but it must be emphasized that documentation of the variability of menstrual cycles is inaccurate and inconsistent when data collection is dependent on information recorded by the working females themselves (64). The preferred assays recommended for the assessment of the ovarian cycle of women in the workplace are daily measurement of salivary or vaginal electrical resistance; mid-cycle urine tests for the surge of luteiniz-

Table 1. Studies on the association between female fertility or related reproductive outcomes and various occupational exposures or occupations.

Occupational exposure or occupation	Reproductive outcome						References
	HI	MD	SA	SB	PD	IN	
Chemical, plastics and rubber industry							
Carbon disulfide		+					(8)
Pharmaceutical workers, viscose rayon industry and styrene manufacturing workers in the Union of Chemical Workers			(+)				(9,10)
Unpacked antibiotics handling						+	(11)
Pharmaceutical workers exposed to estrogens and different solvents			(+)				(12)
Plastic manufacturing						(+)	(13)
Polyvinyl chloride and styrene plastic workers			(+)				(14)
Phthalate plasticizers			(+)				(15)
Plastics and rubber production industry			+				(16)
Synthetic estrogens and progesterons production	(+)	(+)					(17)
	(+)	(-)					(18)
Diethylstilbestrol formulation workers	(+)						(19)
Isoprene synthetic rubber (dimethyldioxane)		(+)					(20)
Styrene		(+)					(20)
		(-)	(-)			(+)	(21)
Caprolactam		(+)					(20)
Manganese compounds		(+)					(20)
Oil-processing (warehouse, laboratory and technological departments workers)	(+)	(+)					(22)
Organic solvents			(+)				(23)
Technical rubber articles production		(+)	(+)				(24)
Polyamide cord (caprone, anid production)		(+)	(+)				(25)
Chemical workers (ammonia, carbamide, CS ₂ , CO, methanol, arsenic, and others)		(+)					(26)
Dry cleaners (tetrachloroethylene)			(-)		(-)	(-)	(27)
			(+)				(28)
Dry-cleaning			(-)			(+)	(29)
			(+)				(30)
Chemical reagents production (acids, bases, oxides, Fe, Cu, Zn, Al, Ca, Ba)			(+)				(31)
Polyvinyl chloride and epoxy plastics production			(+)		(+)		(32)
Rubber industry workers			-				(33)
			(-)				(34)
Rubber footwear department workers			(+)				(34)
Tire department workers			(-)				(34)
Tire builders			(+)				(35)
Machine and metallurgic industry							
Lead (historical data)		(+)	(+)				(36)
Lead						(+)	(13)
			(-)				(37)
Mercury						(+)	(13)
Cadmium						(+)	(13)
Smelter workers (lead, arsenic, SO ₂ , mercury)			(+)				(38)
Steel workers			(-)				(39)
Ferrous metallurgy workers (manganese, lead)		(+)					(40)
Foundry and machine construction workers		(+)	(+)				(41)
Machine tool operators			(+)		(+)		(42,43)
Members of Metal Workers' Union			(+)				(9,10)
Metal industry workers			-				(44)
			+				(45)
Radioelectric industry (soldering, high frequency electromagnetic fields, solvents)		(+)	(+)				(46)
Radio sets production		(+)					(47)
Shipyard workers	(+)	(+)					(48)
Welders						(+)	(13)
Antirust agents						(+)	(13)
Noise						(+)	(13)
Agriculture and food industry							
Cattle breeders		(+)					(49)
Plant protecting agents				(+)			(50)
Butchers, sausagemakers, workers caring for fur-bearing animals			(+)				(44)

(continued)

Table 1. *Continued.*

Occupational exposure or occupation	Reproductive outcome						References
	HI	MD	SA	SB	PD	IN	
Textile industry							
Seamstresses		(+)					(51)
Textile industry workers			(+)				(52)
			+				(45)
			-				(44)
Weavers			+				(44)
Spinners, fabric inspectors, nonspecific occupations related to cutting and sewing			(+)				(44)
Weavers and weaving machine loaders			(+)		(+)		(43)
Textile dyes						(+)	(13)
Wood industry							
Sawmill workers		(+)					(53)
Building and cement industry							
Production of construction elements from reinforced concrete		(+)					(51)
Cement plant workers		(+)				(-)	(54)
Building construction workers			(+)				(55)
Health service units							
Anesthetic gases						(+)	(13)
Operating room staff (anesthetic gases)			(+)				(56)
Chemical sterilizers (ethylene oxide)			+				(56)
Nurses (handling antineoplastic drugs)			+				(56)
Laboratory workers			(+)				(56)
Dentists (mercury vapor)		(+)	(-)				(57)
		(+)	(+)	(+)			(58)
							(59)
Others							
Video display terminal workers (> 20 hr per week)			(+)				(60)
			(-)				(61)
Being employed during pregnancy			(+)				(62)
Heavy lifting			(+)				(63)

Abbreviations: HI, hormonal imbalance; MD, menstrual disorders; SA, spontaneous abortion; SB, stillbirth; PD, premature delivery; IN, infertility; +, positive association; -, no association. The parentheses indicate limitations such as standardization of confounding factors, lack of control group, borderline significance, or small size.

ing hormone; and measurement of progesterone levels in saliva during the luteal phase (65).

Few of the papers reviewed for table 1 attempt to examine the effect of occupational exposure on the ability or inability to conceive, and indeed little research has concentrated on this specific aspect. In Denmark, Rachootin and Olsen (13,66) studied the risk of infertility in relation to occupation using a case-control design. The risk of infertility increased in females who reported exposure to textile dyes, dry cleaning chemicals, noise, lead, mercury and cadmium and in males who had been exposed to heat. The association between chemical exposure and infertility was most convincing among females exposed to textile dyes or to lead, mercury, and cadmium.

The delay to conception was examined as one parameter in another fertility study of Rachootin and Olsen (13), and the cases included were couples who had failed to achieve conception after at least 1 year. There was a significant risk of increased time to conception among women exposed to antirust agents, welding, plastic manufacturing, lead, mercury, cadmium, or anesthetic agents. There was also an increased risk of delay to conception following male exposure to textile dyes, plastic manufacturing, and welding. More recent studies by Bonde (77,78) have confirmed reduced fertility in male welders.

The time to pregnancy has also been investigated among Danish pharmacy assistants (11). Those who unpacked or handled antibiotics had a significant association with delayed pregnancy of at least 12 months, but this was the only medicinal drug exposure which was shown to have such an effect.

Some studies have obtained information about pregnancies and occupational exposure by means of questionnaires, but the response rates to these questionnaires have been fairly low, and the levels of response was different for the exposed and nonexposed individuals, which must be assumed to result in response bias. Many of the investigations relating to operating theater staff are open to bias, but it is not known if such bias is sufficient to account for all the recorded differences in spontaneous abortion rate. The concentrations of anesthetic gases varied and may have been much higher in the past. Therefore, in spite of the likelihood of bias, the possibility of a causal relationship between exposure to anesthetic gases and increased risk of spontaneous abortion cannot be excluded (56).

Further consideration should be given to the use of incidence rates of menstrual disorders and spontaneous abortion as predictors of altered fertility. A new prospective approach using assays for hCG or early pregnancy-associated protein (EPAP) (67) to detect pregnancy at an

Table 2. Studies on the association between male fertility or related reproductive outcomes and various occupational exposures or occupations.

Occupational exposure or occupation	Reproductive outcomes			References
	HI	SA	IN	
Lead	(+)	(+)		(68)
	(+)	(+)		(69)
	(-)	(+)		(70)
		(-)		(71)
		+		(72)
			(+) ^a	(73)
Manganese			(+)	(74)
Alkyl mercury		(+)		(75,76)
Welders			+	(77)
			(+)	(78)
		+		(79)
		(+)		(80)
		-		(81)
	(+)	(+)		(82)
		(-)		(83)
Mercury vapor			(-)	(84)
			(-)	(74)
Antimonite		(+)		(20)
Anesthetic gases			(+)	(85)
			(+)	(86)
			(+) ^a	(87)
Anesthesiologists		-		(88)
Dibromochloropropane			(+)	(89)
	(+)	(+)		(90,91)
		+		(92)
	(+)	(+)		(93)
		+		(94)
Epichlorohydrine	(-)	(-)		(75,76)
		-		(94)
Carbon disulfide		-		(95)
Para-tertiary butyl benzoic acid	-	-		(96)
Chlorodecone (Kaprone)		(+)		(97)
		+		(98)
Carbaryl		(+)		(99)
Chloroprene		(+)		(20)
Organic solvents			(+) ^a	(100)
Oral contraceptives formulation workers	+			(17)
	(+)	(+)		(18)
Diethylstilbestrol formulation workers	(+)			(19)
Painters (exposure to organic solvents)			(+)	(101)
Painters (ethylene glycol ethers)		+		(102)
Ethylene dibromide			(+)	(103)
		(+)		(104)
Heat			(+)	(13)
Radioelectric, textile and typographic industry workers		(+)		(105)
Styrene and acetone (reinforced plastic production)		(+)		(106)
Methylene chloride		(+)		(107)

Abbreviations: HI, hormone imbalance; SA, sperm abnormalities; IN, infertility; +, positive association; -, no association. The parentheses indicate limitations such as standardization of confounding factors, lack of control group, borderline significance, or small size.

^aIncreased risk of spontaneous abortion in wives of exposed men.

early stage could help to differentiate subclinical early spontaneous abortion from menstrual dysfunction.

Occupational Exposure and Male Infertility

The possible impact of occupational agents on the fertility of male workers has been explored only to a limited extent, probably because it has for a long time been assumed that couple infertility or unsuccessful pregnancy outcome was more likely to be linked with female health problems. However, recent evidence, substantiated by animal studies, indicates a high susceptibility of spermatogenesis and spermiogenesis to many toxic substances. Table 2 lists the occupational exposures that have been examined for effects on male fertility and related reproductive outcomes.

The accumulated data suggest that exposure to the following substances or occupational settings may affect the function of part of the male genital system: alkylmercury, antimonite, anesthetic gases, chlorodecone, chloroprene, some carbonates (carbonyl), 1,2-dibromo-3-chloropropane, ethylene glycol ethers, ethylene dibromide, inorganic lead, manganese, methyl chloride, organic solvents, synthetic estrogens and progestogens, combined exposure to styrene and acetone, welding operations, and heat. The outcome of such exposure may be decreased number of spermatozoa in the ejaculate, decreased number of mobile spermatozoa, increased percentage of morphologically anomalous spermatozoa, hyperestrogenism, and male feminizing effects, impotence and infertility and/or increased spontaneous abortion rate in wives of exposed workers.

There are several chemicals that are suspected of affecting libido and/or potency of workers, and the resultant impotence serves to reduce fertility. Among such substances are diaminostilbene (108), manganese, boron, chloroprene (20,109), methyl methacrylate, and vinyl chloride (110,111), tetraethyl lead (112), and carbon disulfide (95,113,114).

The degree of alteration of spermatogenesis and quality of semen depends on the levels of exposure and appears to be reversible after withdrawal from exposure. However, reversibility is less likely after exposure to dibromochloropropane (DBCP). A follow-up study 7 years after DBCP exposure revealed that only one of the eight workers who were originally rendered azoospermic recovered a normal sperm count, and one further individual showed partial recovery achieving oligozoospermia (92). This result suggests that permanent destruction of the germinal epithelium occurred.

Evaluation of Existing Data

Henderson et al. (75,76) have emphasized that only a few studies investigating reproductive toxins have fulfilled the criteria for good study design. These criteria are *a*) the power of the study should be adequate (at least 80%), necessitating a sufficiently large sample size; *b*) the study

should be designed to show a dose-response effect in order to demonstrate a causal relationship; *c*) the many forms of bias, including selection, recall, and observation bias, should be controlled and minimized; and *d*) the confounding factors should also be controlled and minimized.

The potential confounding factors were not considered as often as they should have been in the papers reviewed. Reproductive outcomes may vary according to socioeconomic status, maternal age, and smoking and drinking habits, therefore, studies ought to make allowance for these factors, but only a few do so adequately. It must also be remembered that the effects of occupational exposure may be much more subtle than the effects of behavioral and demographic factors. As an example, in the assessment of sperm density only a few studies have adjusted for the marked variation in the abstinence period, although this is a factor that has a marked effect on sperm count.

Only a few studies have included an estimate of their power to detect a meaningful effect. This limitation is reflected in the preponderance of negative or conflicting results in the studies summarized in the tables of this review article. The investigation of fertility and of the influence of occupational exposure on fertility and sexuality has begun only quite recently. At the present, it is not possible to estimate the importance of the influence of occupational factors on fertility and sexuality, although some definitely harmful agents have been identified. The combination of the entire spectrum of different methods used to study reproductive toxicants will probably give more information in the future.

Conclusions

Recommendations formulated to safeguard workers during their reproductive age should be based on the thorough assessment of the potential impact of environmental and occupational factors on sexuality and fertility. These factors include chemicals, physical agents (ionizing radiation, electromagnetic fields, noise, vibration, ambient temperature), biological organisms (bacteria, viruses), physical load, and position at work.

A number of points have been identified in this paper and on the basis of these, recommendations can be made.

1. Fertility as a complex biological phenomenon and the assessment of the effects of environmental factors require a multidisciplinary approach at work sites (industrial plants) and at regional and national levels.
2. It must be stressed that only a few chemicals can definitely be incriminated as being reproductive toxic agents in humans, but in experimental studies in animals a large number of chemicals have been shown to have an adverse effect on reproduction, and many more have not yet been examined.
3. Organizations responsible for planning research at national and international levels should set priorities for research into work-related causes of infertility. Better coordination of such studies is required and there is a need for the development of standardized methods.

4. There is a requirement for a leading WHO collaborating center which could coordinate stimulation of national and international collaborative studies in work-related reproductive failures; collection and evaluation of relevant information on the impact of industrial chemicals and other occupational factors on reproductive outcomes on the basis of international and interorganizational coordination of such activities; setting of priorities and criteria for the evaluation of the effects of potentially hazardous agents on reproduction; initiation of training programs; initiation and coordination of international exchanges of information on reproductive hazards in order to improve the quality of industrial hygiene guidelines; and development of collaboration with national centers dealing with similar problems.
5. Infertility has many causes, and only a proportion of these are related to occupational factors. A standard research protocol would be useful to assure a better quality of research.
6. Chemicals exhibiting genetic toxicity should be considered not only as potential carcinogens but also as possible reproductive toxicants. Verification and validation of experimental data through well-designed epidemiological studies are needed in this field.
7. There is a need for international evaluation of occupational factors affecting human reproduction to prepare criteria for their classification and risk assessment and to produce a list of agents hazardous to reproduction.
8. Administrative guidelines for the working environment, such as permissible exposure limits, should be based on data referring to the effects on both male and female reproductive processes.
9. Workers should be informed personally of the effects of the reproductive hazards to which they are exposed.
10. A health examination, which is obligatory in many countries as part of the occupation health care program, should include an assessment of reproductive health.
11. The potential impact of occupational factors on sexuality and fertility should be considered in order to keep the working environment safe for the reproductive health of both men and women.

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